IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Albert B. Deisseroth, et al.

Application No.: 10/534,605 Confirmation No.: 7449

Filed: May 11,2005 Art Unit: 1644

For: Adenoviral Vector Vaccine Examiner: Phillip Gambel

RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
Mail Stop Amendment
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the restriction requirement set forth in the Office Action mailed October 5, 2009, Applicants hereby elect Group I independent claim 1, with traverse, for continued examination. Linking dependent claims 2 through 12 shall also be examined. This independent and the elected dependent claims are hereby identified as the claims encompassing the elected invention.

In paragraph 3 of the Detailed Action, the Examiner has required restriction between:

Group I. Claims 1-12, drawn to an adenoviral expression vector comprising a tumor antigen and CD40L.

Group II. Claims 13-34, drawn to methods of generating an immune response to a tumor antigen, treating cancer to a tumor antigen or generating an immune response to an infection with papilloma virus with an adenoviral expression vector comprising a tumor antigen (e.g., B7 protein of human papilloma virus) and CD40L.

Applicants make the election of Group I without prejudice to, or disclaimer of, subject matter recited in the Group II non-elected claims. Applicants expressly reserve their rights to prosecute the non-elected claims in a subsequent application.

The Examiner contends that the inventions listed as Groups I and II do not relate to a single general inventive concept under the PCT Rule 13.1 because, under PCT Rule 13.2, they allegedly lack the same or corresponding special technical features. The Examiner alleges that the technical feature shared by Groups I and II (an adenoviral vector comprising a tumor antigen, e.g. papilloma viral protein, and CD40L) is not a special feature as it does not make a contribution over the prior art in view of Curiel et al. (US Patent No. 6,284,742) and/or Mc Cown et al. (US Patent No. 7,071,172). The Examiner alleges that this technical feature of Groups I and II cannot be a "special technical feature" unifying the claim groups because the technical feature is allegedly shown to be in the prior art.

As advanced below, applicants respectfully submit that the application claims do relate to one invention only or to a group of inventions so linked as to form a single general inventive concept

Product claim 1 calls for an adenoviral expression vector for generating immunity against a tumor antigen, said vector comprising a transcription unit encoding a polypeptide, said polypeptide comprising from the amino terminus a secretory signal sequence, a tumor antigen, and CD40 ligand, wherein said tumor antigen is different from CD40 ligand and wherein said CD40 ligand is missing all or substantially all of the transmembrane domain rendering the CD40L secretable.

In turning to the two patents cited by the Examiner, in brief, Curiel et al. and McCown et al. each teaches a technology distinct from that of applicants and neither of these references, whether separately or in combination, anticipates the adenoviral expression vector product claim set forth in claim 1.

First, with respect to distinguishing Curiel et al. from applicants' invention, as stated in applicants' claim 1, applicants' CD40 ligand is missing all or substantially all of the transmembrane domain rendering the CD40L secretable. This acts to help mobilize antigen specific CD40 effector cells to expand and to course through the bloodstream to locations of cancer or infection. This is nowhere found or taught in the Curiel et al. patent which uses a technology that is it believed to be distinct from and leads away from that of applicants. For example, the Curiel et al. patent does not use secretion in the sense of applicants invention. Moreover, the Curiel et al. patent primarily teaches the use of a bispecific antibody (not used by applicants) with affinities for the adenovirus fiber knob and a dendritic cell (See column 2 - Summary of the Invention). In addition, for example, contrary to the Examiner's statement, in the Curiel et al. patent, the CD40L protein is not internal to the vector (See column 2 lines 44-51 and column 4 lines 16-30 of Curiel et al.), as opposed to the recitation in applicants' claim 1 which calls for the CD40L attached to a tumor antigen which is inserted into the transcription unit of the vector. In Curiel et al., the adenoviral vectors are targeted to the CD40 receptor on dendritic cells as opposed to applicants' invention. Moreover, in the Curiel et al. patent the CD40L is attached to the outside of the vector and not to the tumor antigen in the transcription unit (see above references in the Curiel et al. patent). Cruiel et al. also, as a further example, genetically manipulates dendritic cells and B cells (See the Abstract). Applicants' invention, in contrast with the teachings in Curiel et al., does not genetically manipulate dendritic cells (as is practiced by Curiel et al.) but infects non-dendritic cells by the adenoviral vector in the subcutaneous space to activate dendritic cells, as well as T cells and B cells. Applicant's infected cells release the tumor antigen CD40L fusion protein. The released fusion protein is then free to bind to the dendritic cells to activate them and to antigen load them unlike in the Curiel et al. patent. More particularly, the invention of Curiel's et al.'s patent is limited in that CD40L is not included in the transcription unit inserted in the virus (as claimed by applicants), and accordingly limiting each virus particle to infect no more than one dendritic cell

With respect to the McCown et al. patent '172, the McCown et al. patent specification fails, for example, to disclose employment of a viral vector carrying a transcription unit which encodes a polypeptide composed of a target antigen linked to the CD40 ligand from which the

transmembrane domains have been removed and attaching it to an antigen in order to make the target antigen more immunogenic. Instead, the viral vector strategy of McCown, disclosed in the McCown patent specification, uses the vector to program cells infected by the viral vector carrying a CD40L transcription unit to produce CD40L inside the target cell. In this version, although the transcription unit carried by the viral vectors of McCown have a secretory sequence preceding the CD40L, because the transmembrane domain of the CD40L has been left in the McCown version, the CD40L will never be released from the infected cell but will become a part of the plasma membrane. Thus, for example, are addressed two differences between the viral vectors of McCown and the applicants. First, for example, in applicants' vector, the CD40L is attached to a target antigen in order to make the target antigen more immunogenic And, second, for example, only the extracellular domain of the CD40L is present in the applicants vector (without any transmembrane domain) whereas the entire CD40L is in the transcription unit of the McCown vector.

In addition, for example, as is evident from numerous sections in the specification (also see claim1) McCown teaches an invention that has to do with, for example, an adeno-associated virus (AAV), not an adenovirus claimed by applicants, which adeno-associated virus carries a secretory signal linked to a peptide that stabilizes the neurons and prevents them from discharging thereby preventing seizures. There are very major structural and functional differences between an adenovirus and an adeno-associated virus and between an adenoviral vector and an adenovirus associated vector. For example, an adenovirus can make copies of itself whereas an adeno-associated virus cannot make copies of itself without the help of other viruses. Another example is that the adenovirus, in size, is a large multiple of the AAV thereby limiting the size of antigens that can be utilized with AAV yet can be used with the adenovirus. A further example is that an AAV goes into the DNA of a host cell permanently while an adenovirus does not. Yet another difference is that the AAV is not immunogenic whereas the adenovirus is immunogenic. Other important functional and structural differences exist. Although McCown may, in passing, refer to an adenovirus, nowhere in the McCown et al. patent is there a teaching of how to implement the unique structurally and functionally different adenovirus in the McCown specification. Accordingly, contrary to the Examiner's allegation that McCown teaches adenoviral delivery

vectors, one simply has no teaching from the specification how to implement an adenovirus vector in McCown in place of the AAV vector to take into consideration the various differences between the two viruses.

Last but not least in paragraph 2 of the Detailed Action of the Examiner's Office Action under the heading **REQUIREMENT FOR UNITY OF INVENTION**, as provided for in 37 CFR 1.475(b),it states that a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories. In this regard, the Examiner's attention is directed to category (2) specifying a product and process of use of said product. With respect to applicants claims, in each of method claims 13 and 31, the method comprises"...administering to the individual an effective amount of the adenoviral expression vector of claim1". Accordingly, it is respectfully submitted that applicants product claim 1 and method claims 13 and 31 fall within category (2).

For the reasons advanced above applicants respectfully submit that the restriction requirement set forth by the Examiner be waived. Accordingly, applicants respectfully request examination of claims 1-34.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 50-4752. To the extent necessary, a petition for extension of time under 37 C.F.R.§ 1.136 is hereby made, the fee for which should be charged to the aforementioned account.

Dated: March 30, 2010

Respectfully submitted,

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